UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,603	12/19/2001	Napoleone Ferrara	GENENT.1516CP1	4344

7590 11/18/2005

DENISE M. KETTELBERGER, Ph.D
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/027,603	FERRARA ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58,80-87,89,90,93-104 and 106-108* is/are pending in the application.

4a) Of the above claim(s) *58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *80-87,89,90,93 and 106-108* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 58, 80-87, 89-90, 93-104, and 106-108 are pending.

2. Claim 58 stands withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to a non-elected invention.

3. Claims 80-87, 89-90, 93-104 and 106-108 are being acted upon in this Office Action.

4. Claim 80 is objected to because "antibody fragment" should have been "antibody fragment thereof".

5. Claim 89 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 83. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

6. Applicant is advised that should claim 83 be found allowable, claim 89 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 93 and 101 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The "antibody or antibody fragment thereof specifically binds a polypeptide comprising the amino acid sequence of SEQ ID NO: 2" in claim 93 is indefinite and ambiguous because the antibody and binding fragment thereof binds residues 20-105 of SEQ ID NO: 2 in claim 80 and

now the antibody and fragment thereof suddenly binds extra amino acids residues 1-19 in polypeptide comprising the amino acid sequence of SEQ ID NO: 2. It is suggested that claim 93 be rewritten in independent form.

The "humanized antibody or humanized antibody fragment" in claim 101 has no antecedent basis in base claim 100 because the word "humanized antibody" is not recited in base claim 100.

9. Claim 108 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for an antibody or antibody fragment thereof that specifically binds residues 20-105 of SEQ ID NO: 2 and inhibits EG-VEGF induced proliferation of endothelial cells, (2) the said antibody or binding fragment thereof wherein the antibody or antibody fragment is selected from the group consisting of a monoclonal antibody, a chimeric antibody, a humanized antibody or binding fragment thereof, (3) the said antibody or antibody fragment wherein the antibody fragment is selected from the group consisting of Fab, Fab', F(ab')2 and Fv fragment, (4) the said antibody or antibody fragment thereof wherein the monoclonal antibody is produced by a hybridoma having ATCC accession number PTA-4119, PTA-4120, PTA-4121 or PTA-4122, **does not** reasonably provide enablement for any antagonist of EG-VEGF, wherein the antagonist "comprises" an antibody or antibody fragment that specifically binds a polypeptide comprising SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only four monoclonal antibodies 1C6, 2A3, 2A8 and 4H9 produced by hybridoma having the accession number PTA-4119, PTA-4120, PTA-4121 or PTA-4122, respectively, that bind specifically to human EG-VEGF comprising SEQ ID NO: 2 or

residues 20-105 of SEQ ID NO: 2 as shown in Figure 21 for diagnostic assays. The specification discloses only two monoclonal antibodies 1C6 and 4H9 have neutralizing activity using a cell-based proliferation assays (See Figure 21, see error bar). The specification discloses the EG-VEGF or VEGF antagonist may, for example be an anti-EG-VEGF or anti-VEGF antibody, respectively, specifically including antibody fragment (page 7).

The specification does not teach how to make any and all antagonist of EG-VEGF because the term "comprising" is open-ended. It expands the antibody or antibody fragment thereof that specifically binds a polypeptide comprising SEQ ID NO: 2 to include additional amino acids at either or both ends. There is insufficient guidance as to which amino acids or polypeptide to be added to the antibody or antibody fragment thereof in the claimed EG-VEGF antagonist.

Stryer *et al*, of record, teach that a protein is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages).

Ngo *et al*, of record, teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Given the unlimited number of amino acids or polypeptide to be added to the antibody, it is unpredictable which undisclosed polypeptide is useful for which purpose.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Note, amending claim 108 to recite an antagonist of EG-VEGF wherein the antagonist is an antibody or antibody fragment that specifically binds polypeptide comprising SEQ ID NO: 2 and inhibits EG-VEGF induced proliferation of endothelial cells would obviate this rejection.

10. Claim 108 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of any antagonist of EG-VEGF, wherein the antagonist "comprises" an antibody or antibody fragment that specifically binds a polypeptide comprising SEQ ID NO: 2.

The specification discloses only four monoclonal antibodies 1C6, 2A3, 2A8 and 4H9 produced by hybridoma having the accession number PTA-4119, PTA-4120, PTA-4121 or PTA-4122, respectively, that bind specifically to human EG-VEGF comprising SEQ ID NO: 2 or residues 20-105 of SEQ ID NO: 2 as shown in Figure 21 for diagnostic assays. The specification discloses only two monoclonal antibodies 1C6 and 4H9 have neutralizing activity using a cell-based proliferation assays (See Figure 21, see error bar). The specification discloses the EG-VEGF or VEGF antagonist may, for example be an anti-EG-VEGF or anti-VEGF antibody, respectively, specifically including antibody fragment (page 7).

The specification does not teach adequately describe any and all antagonist of EG-VEGF as set forth in claim 108 because the term "comprising" is open-ended. It expands the antibody or antibody fragment thereof that specifically binds a polypeptide comprising SEQ ID NO: 2 to include additional amino acids at either or both ends. There is insufficient written description about which amino acids or polypeptide to be added to the antibody or antibody fragment thereof in the claimed EG-VEGF antagonist. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of compound to be added to the claimed antibody or antibody fragment thereof that specifically to SEQ ID NO: 2 to describe the genus for the claimed EG-VEGF antagonist. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Note, amending claim 108 to recite an antagonist of EG-VEGF wherein the antagonist is an antibody or antibody fragment that specifically binds polypeptide comprising SEQ ID NO: 2 and inhibits EG-VEGF induced proliferation of endothelial cells would obviate this rejection.

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 80-87, 89-90, 93, and 106-108 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-17 of copending Application No. 10/305,654. Although the conflicting claims are not identical, they are not patentably distinct from each other because the species of antibodies to EG-VEGF such as monoclonal, humanized, chimeric and binding fragment thereof that binds specifically to EG-VEGF comprising SEQ ID NO: 2 or from residues 20-105 of SEQ ID NO: 2 anticipate the genus of antibody that specifically binds to SEQ ID NO: 172 of copending application 10/431,805. The polypeptide of SEQ ID NO: 172 of copending application is 100% identical to instant polypeptide of SEQ ID NO: 2. The antibody made using either polypeptide would bind to each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Claims 85, 100, 106 and 107 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

16. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
November 10, 2005

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600